

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Schiemann et al.

Group Art Unit: 1625

Serial No.: 10/583,689

Examiner: Rita J. Desai

Filed: Dec. 14, 2004

For: 2-(Hetero)-aryl substituted tetrahydrochinoline

DECLARATION UNDER 37 C.F.R. § 1.132

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

SIR:

Frank Zenke, being duly warned, deposes and says:

I am a citizen of Germany residing at Darmstadt, Germany;

I am a biologist by training and experience;

the degree of Dr. rer. nat. was bestowed on me by the Heinrich-Heine University of Düsseldorf, Germany in 1995;

from 1995 to 1996 I was employed at the Institute for Microbiology, Heinrich-Heine University of Düsseldorf, Germany and the Institute for Genetics, Martin-Luther University Halle;

from 1997 to 2001 I was postdoctoral scientist at the Department of Immunology, The Scripps Research Institute, La Jolla, USA;

since October 2001 I am an employee at Merck KGaA, Darmstadt, Germany;

I am author or co-author of several papers and patents in the fields of biochemistry and cell biology.

The test results presented below for the present application support that the claimed compounds are inhibitors of the mitotic motor protein Eg5.

I have carried out, or supervised experiments for testing these inhibitors according to the methods described within the genus claimed in the pending application.

Pharmacological Report

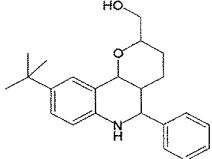
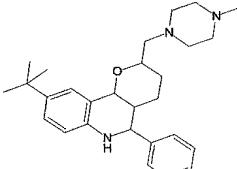
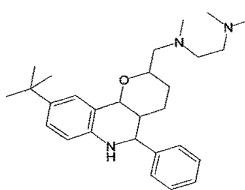
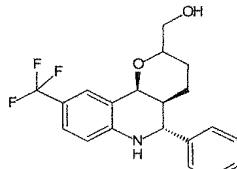
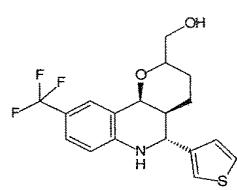
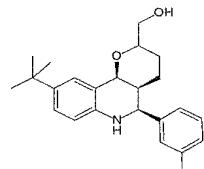
HCT116 cell viability / proliferation assay

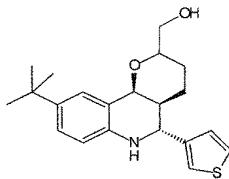
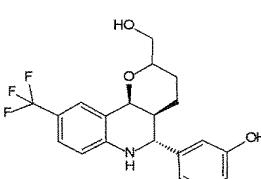
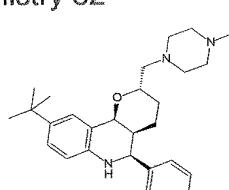
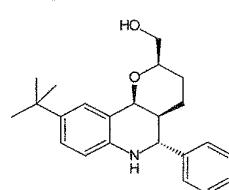
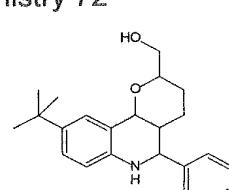
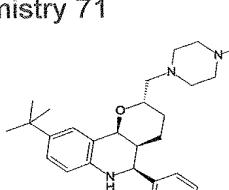
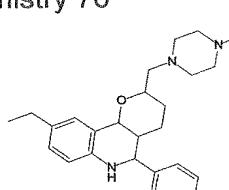
The proliferation data have been obtained by means of a conventional assay, which was known to the skilled artisan for the measurement of such biological data at the date of filing this application. Human colon carcinoma cells (HCT116, ATCC CCL 247) were cultured at 37°C and 10% CO₂ in MEM alpha (Invitrogen, #22571) supplemented with 10% (v/v) heat-inactivated fetal bovine serum (Pan Biotech, #3302), 2mM glutamine (Invitrogen, #25030) and 1mM sodium pyruvate (Invitrogen, #11360). Cells were detached from F75 cell culture flasks (Nunc 734 2066) with trypsin/EDTA (Invitrogen, #15400), counted using a Thoma chamber (VWR, #631-1117), and plated in 96-well microtiter plates (Falcon 353227) in fresh medium (cell density of HCT116: 1*10⁴ cells in 0.1ml medium per cavity). Cells were cultured overnight and treated on the next day with Eg5 inhibitors or with vehicle alone (0.5% DMSO; Merck, #1.02931) for 48hrs. Wells containing culture medium alone served as background controls.

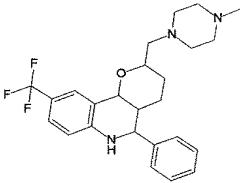
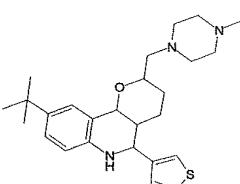
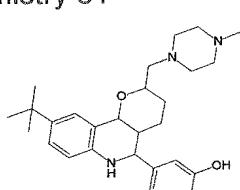
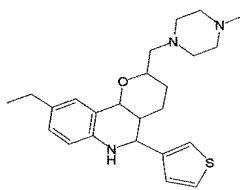
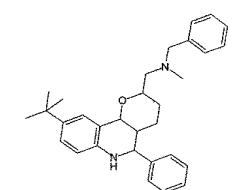
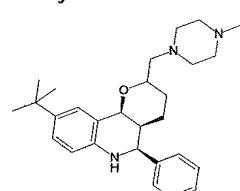
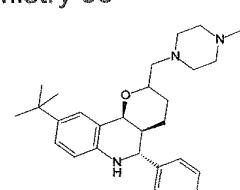
At the end of compound incubation the medium was discarded, the remaining attached cells were washed once with 1x PBS (Life Technologies 14190-094), and stained for 15 minutes with crystal violet solution (0.5% crystal violet, 20% methanol). Subsequently, the wells were washed thoroughly with deionised water until no colour clouds came off the cells. The plates were dried at room temperature overnight or in a 37°C incubator for at least one hour. The bound crystal violet was extracted with 200µl methanol per well and absorption was measured at 550nm wavelength in a spectrophotometer (Tecan Reader SLT Rainbow, Berthold Reader Mithras, LB 940). The mean absorption value of the medium controls was subtracted from all other wells. DMSO control treated cells served as positive control (100%). IC₅₀ values were determined using a curve fitting algorithm of the statistics program RS/1 (Brooks Automation Inc., Massachusetts).

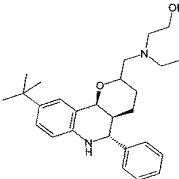
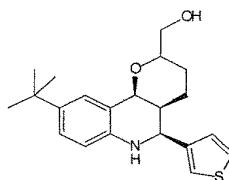
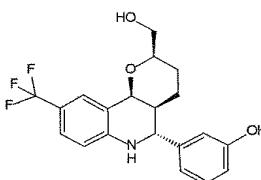
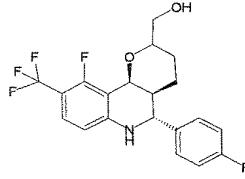
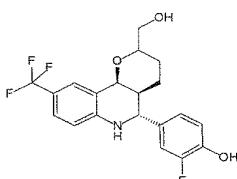
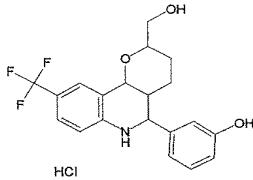
The test data of the Pharmacological Report (Table I) show the compounds tested and their IC₅₀-values. The "no." refers to present application where compounds are disclosed.

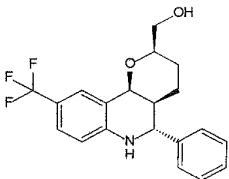
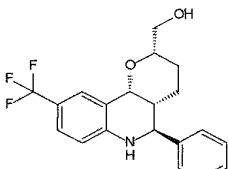
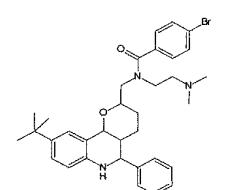
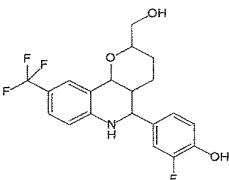
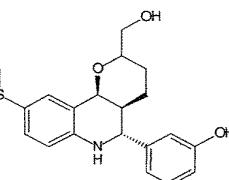
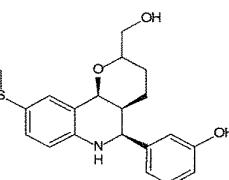
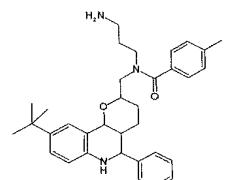
Table I: IC₅₀ values for inhibiting Eg5

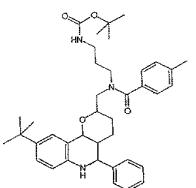
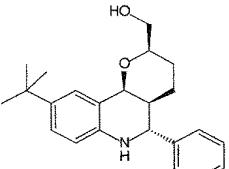
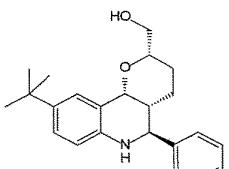
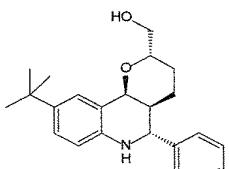
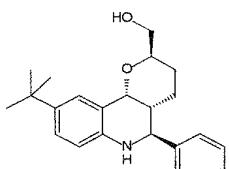
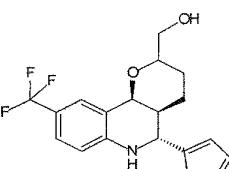
No.	CHEMISTRY	NAME	Proliferation IC ₅₀ [M]
60		(9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	4,30E-08
	Chemistry 37		
89		9-tert-Butyl-2-(4-methyl-piperazin-1-ylmethyl)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline	6,60E-07
	Chemistry 354		
96		N-(9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-N,N',N'-trimethyl-ethane-1,2-diamine	3,90E-07
	Chemistry 346		
120		((4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,20E-07
	Chemistry 89		
121		((4aS,5R,10bS)-5-Thiophen-3-yl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	3,42E-07
	Chemistry 88	.	
122		3-((4aS,5S,10bS)-9-tert-Butyl-2-hydroxymethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	1,10E-06
	Chemistry 87		

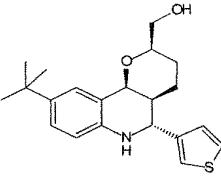
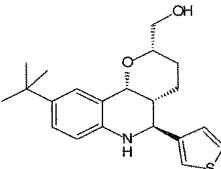
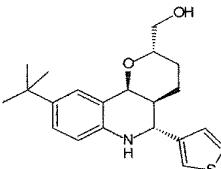
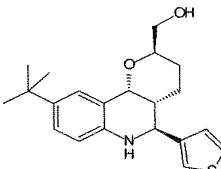
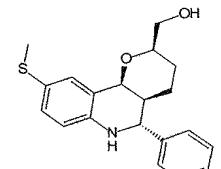
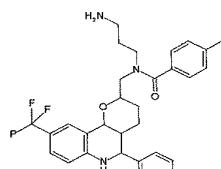
126		((4aS,5R,10bS)-9-tert-Butyl-5-thiophen-3-yl-3,4,4a,5,6,10b-hexahydro-2H-pyran-2-yl)-methanol	2,64E-08
Chemistry 83			
127		3-((4aS,5R,10bS)-2-Hydroxymethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-2-yl)-phenol	5,80E-08
Chemistry 82			
133		(2S,4aS,5S,10bS)-9-tert-Butyl-2-(4-methyl-piperazin-1-ylmethyl)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-2-yl)quinoline	4,10E-07
Chemistry 76			
137		((2R,4aS,5R,10bS)-9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-2-yl)-methanol	2,60E-08
Chemistry 72			
138		(9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-2-yl)-methanol	3,04E-08
Chemistry 71			
139		(2S,4aS,5S,10bS)-9-tert-Butyl-2-(4-methyl-piperazin-1-ylmethyl)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-2-yl)quinoline	8,00E-07
Chemistry 70			
145		9-Ethyl-2-(4-methyl-piperazin-1-ylmethyl)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-2-yl)quinoline	1,10E-06
Chemistry 63			

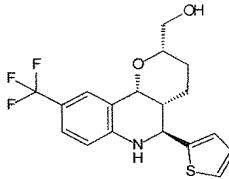
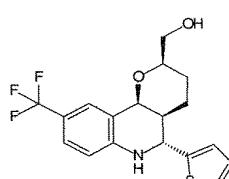
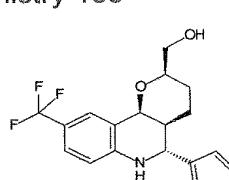
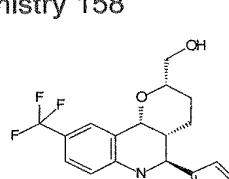
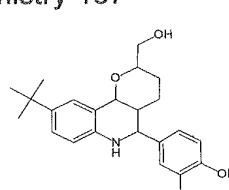
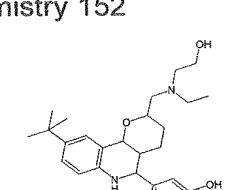
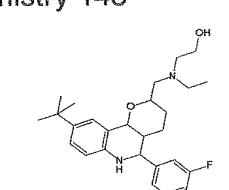
146		2-(4-Methyl-piperazin-1-ylmethyl)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyranopyrano[3,2-c]quinoline	3,30E-06
Chemistry 62			
147		9-tert-Butyl-2-(4-methyl-piperazin-1-ylmethyl)-5-thiophen-3-yl-3,4,4a,5,6,10b-hexahydro-2H-pyranopyrano[3,2-c]quinoline	1,10E-06
Chemistry 61			
148		3-[9-tert-Butyl-2-(4-methyl-piperazin-1-ylmethyl)-3,4,4a,5,6,10b-hexahydro-2H-pyranopyrano[3,2-c]quinolin-5-yl]-phenol	2,40E-07
Chemistry 60			
150		9-Ethyl-2-(4-methyl-piperazin-1-ylmethyl)-5-thiophen-3-yl-3,4,4a,5,6,10b-hexahydro-2H-pyranopyrano[3,2-c]quinoline	4,30E-06
Chemistry 58			
151		Benzyl-(9-tert-butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyranopyrano[3,2-c]quinolin-2-ylmethyl)-methyl-amine	6,70E-06
Chemistry 57			
153		(4aS,5S,10bS)-9-tert-Butyl-2-(4-methyl-piperazin-1-ylmethyl)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyranopyrano[3,2-c]quinoline	2,80E-06
Chemistry 55			
154		(4aS,5R,10bS)-9-tert-Butyl-2-(4-methyl-piperazin-1-ylmethyl)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyranopyrano[3,2-c]quinoline	1,50E-07
Chemistry 54			

159		2-[((4aS,5R,10bS)-9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-ethyl-amino]-ethanol	1,10E-07
Chemistry 49			
167		((4aS,5S,10bS)-9-tert-Butyl-5-thiophen-3-yl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	3,30E-07
Chemistry 321			
193		3-((2R,4aS,5R,10bS)-2-Hydroxymethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	8,00E-08
Chemistry 131			
199		[(4aS,5R,10bS)-10-Fluoro-5-(4-fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	2,10E-06
Chemistry 126			
200		2-Fluoro-4-((4aS,5R,10bS)-2-hydroxymethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	4,00E-08
Chemistry 125			
209		3-(2-Hydroxymethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	2,40E-08
Chemistry 586			

225		((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol 5,67E-08
Chemistry 104		
226		((2S,4aR,5S,10bR)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol 2,60E-05
Chemistry 103		
227		4-Bromo-N-(9-tert-butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)methyl)-N-(2-dimethylamino-ethyl)-benzamide 1,20E-05
Chemistry 102		
228		2-Fluoro-4-(2-hydroxymethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol 6,40E-08
Chemistry 101		
237		3-((4aS,5R,10bS)-2-Hydroxymethyl-9-methylsulfanyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol 2,60E-07
Chemistry 289		
238		3-((4aS,5S,10bS)-2-Hydroxymethyl-9-methylsulfanyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol 9,80E-07
Chemistry 288		
243		N-(3-Amino-propyl)-N-(9-tert-butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)methyl)-4-methylbenzamide 2,20E-06
Chemistry 283		

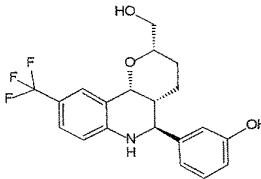
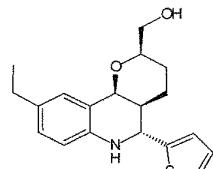
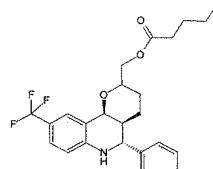
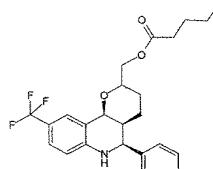
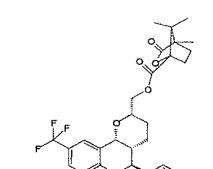
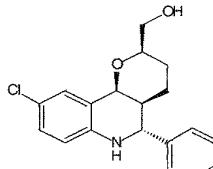
244		{3-[(9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)methyl]- (4-methyl-benzoyl)-amino}-propyl}carbamic acid tert-butyl ester	
Chemistry 282			
248		((2R,4aS,5R,10bS)-9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	8,23E-09
Chemistry 277			
249		((2S,4aR,5S,10bR)-9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,80E-05
Chemistry 276			
250		((2R,4aR,5R,10bR)-9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,70E-06
Chemistry 275			
251		((2S,4aS,5S,10bS)-9-tert-Butyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,30E-05
Chemistry 274			
252		((4aS,5R,10bS)-5-Thiophen-2-yl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,80E-07
Chemistry 273			

265		((2R,4aS,5R,10bS)-9-tert-Butyl-5-thiophen-3-yl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-methanol	3,30E-08
Chemistry 588			
266		((2S,4aR,5S,10bR)-9-tert-Butyl-5-thiophen-3-yl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-methanol	7,40E-06
Chemistry 589			
267		((2S,4aS,5R,10bS)-9-tert-Butyl-5-thiophen-3-yl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-methanol	1,00E-06
Chemistry 590			
268		((2R,4aR,5S,10bR)-9-tert-Butyl-5-thiophen-3-yl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-methanol	5,00E-05
Chemistry 591			
271		((2R,4aS,5R,10bS)-9-Methylsulfanyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-methanol	3,30E-07
Chemistry 164			
272		N-(3-Amino-propyl)-4-methyl-N-(5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-benzamide	2,60E-06
Chemistry 163			

275		((2S,4aR,5S,10bR)-5-Thiophen-2-yl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl) methanol	6,90E-07
Chemistry 160			
276		((2R,4aS,5R,10bS)-5-Thiophen-2-yl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl) methanol	3,10E-08
Chemistry 159			
277		((2R,4aS,5R,10bS)-5-Thiophen-3-yl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl) methanol	1,19E-07
Chemistry 158			
278		((2S,4aR,5S,10bR)-5-Thiophen-3-yl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl) methanol	
Chemistry 157			
283		4-(9-tert-Butyl-2-hydroxymethyl-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-2-fluoro-phenol	6,00E-08
Chemistry 152			
287		3-(9-tert-Butyl-2-{[ethyl-(2-hydroxy-ethyl)-amino]-methyl}-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-phenol	1,50E-08
Chemistry 148			
288		4-(9-tert-Butyl-2-{[ethyl-(2-hydroxy-ethyl)-amino]-methyl}-3,4,4a,5,6,10b-hexahydro-2H-pyran-3-yl)-2-fluoro-phenol	2,70E-08
Chemistry 147			

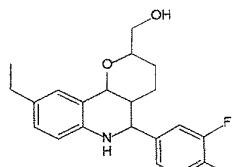
292		((2R,4aS,5R,10bS)-5-Furan-2-yl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	5,10E-07
Chemistry 143			
293		((2R,4aS,5R,10bS)-9-Chloro-5-thiophen-2-yl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,90E-07
Chemistry 142			
301		(4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline-2-carboxylic acid	1,10E-05
Chemistry 592			
304		2-[Ethyl-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethanol	2,47E-07
Chemistry 593			
305		2-[Ethyl-((2S,4aS,5S,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethanol	1,60E-05
Chemistry 594			
309		4,7,7-Trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	5,10E-08
Chemistry 259			

310		3-((4aR,5S,10bR)-9-tert-Butyl-2-hydroxymethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	1,40E-08
Chemistry 595			
315		((2R,4aS,5R,10bS)-9-tert-Butyl-5-thiophen-2-yl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	6,30E-09
Chemistry 254			
319		((2R,4aS,5R,10bS)-9-tert-Butyl-5-thiophen-2-yl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,50E-08
Chemistry 250			
320		((2S,4aR,5S,10bR)-9-tert-Butyl-5-thiophen-2-yl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,90E-06
Chemistry 249			
323		4-(2-Hydroxymethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	2,10E-07
Chemistry 246			
324		3-(9-Ethyl-2-hydroxymethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	3,10E-08
Chemistry 245			
327		3-((2R,4aS,5R,10bS)-2-Hydroxymethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	4,50E-08
Chemistry 242			

328		3-((2S,4aR,5S,10bR)-2-Hydroxymethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-phenol	1,00E-05
Chemistry 241			
329		((2R,4aS,5R,10bS)-9-Ethyl-5-thiophen-2-yl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	1,80E-08
Chemistry 240			
330		Pentanoic acid (4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	3,40E-07
Chemistry 239			
331		Pentanoic acid (4aS,5S,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	1,10E-05
Chemistry 238			
334		4,7,7-Trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylic acid (2S,4aR,5S,10bR)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	5,80E-06
Chemistry 193			
335		((2R,4aS,5R,10bS)-9-Chloro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methanol	9,80E-07
Chemistry 192			

336		Pentanoic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	5,80E-08
Chemistry 191			
337		Pentanoic acid (2S,4aR,5S,10bR)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	3,20E-05
Chemistry 190			
338		Acetic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	2,40E-08
Chemistry 189			
339		Acetic acid (2S,4aR,5S,10bR)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	2,80E-05
Chemistry 188			
340		((2R,4aS,5R,10bS)-9-Ethyl-5-thiophen-2-yl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)methanol	1,50E-08
Chemistry 186			
341		((2S,4aR,5S,10bR)-9-Ethyl-5-thiophen-2-yl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)methanol	2,70E-06
Chemistry 185			

342

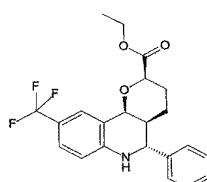


4-(9-Ethyl-2-hydroxymethyl-
3,4,4a,5,6,10b-hexahydro-2H-
pyrano[3,2-c]quinolin-5-yl)-2-
fluoro-phenol

2,00E-08

Chemistry 184

345

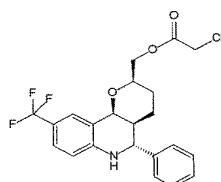


(2R,4aS,5R,10bS)-5-Phenyl-9-
trifluoromethyl-3,4,4a,5,6,10b-
hexahydro-2H-pyrano[3,2-
c]quinoline-2-carboxylic acid ethyl
ester

1,70E-06

Chemistry 175

348

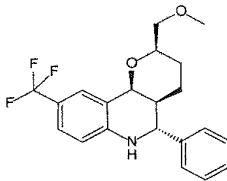


Chloro-acetic acid
(2R,4aS,5R,10bS)-5-phenyl-9-
trifluoromethyl-3,4,4a,5,6,10b-
hexahydro-2H-pyrano[3,2-
c]quinolin-2-ylmethyl ester

2,50E-08

Chemistry 219

349

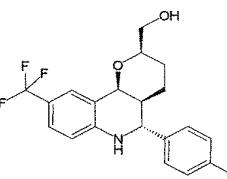


(2R,4aS,5R,10bS)-2-
Methoxymethyl-5-phenyl-9-
trifluoromethyl-3,4,4a,5,6,10b-
hexahydro-2H-pyrano[3,2-
c]quinoline

1,00E-07

Chemistry 215

350

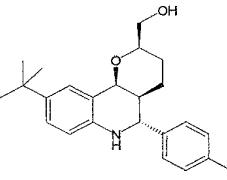


[(2R,4aS,5R,10bS)-5-(4-Fluoro-
phenyl)-9-trifluoromethyl-
3,4,4a,5,6,10b-hexahydro-2H-
pyrano[3,2-c]quinolin-2-yl]-
methanol

1,00E-06

Chemistry 214

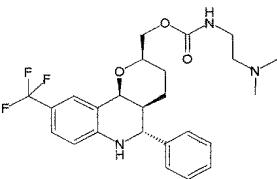
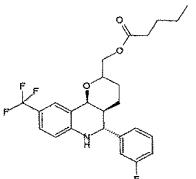
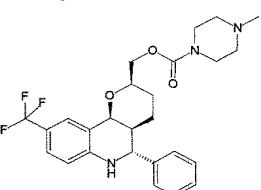
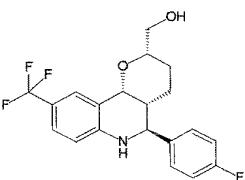
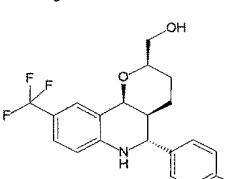
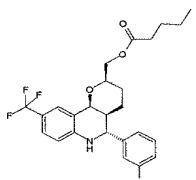
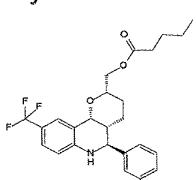
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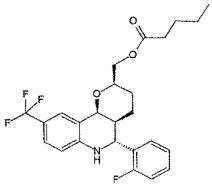
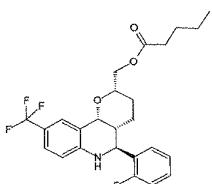
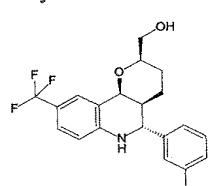
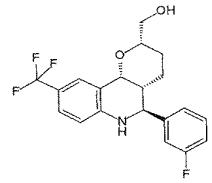
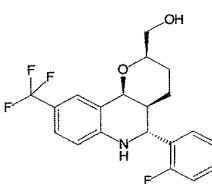
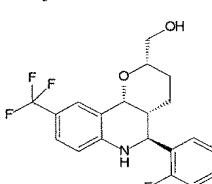
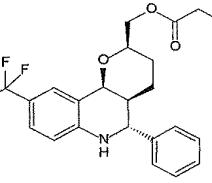


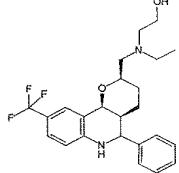
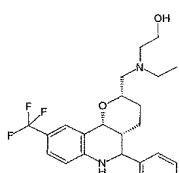
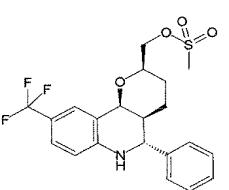
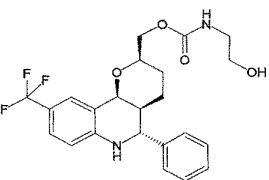
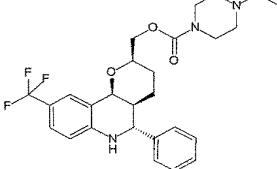
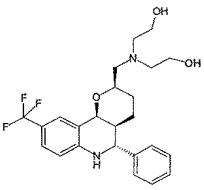
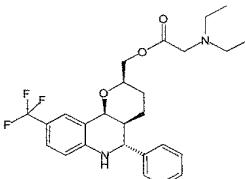
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c]quinolin-2-yl]-methanol

4,00E-07

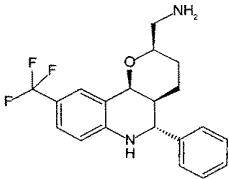
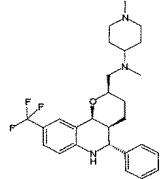
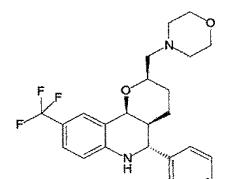
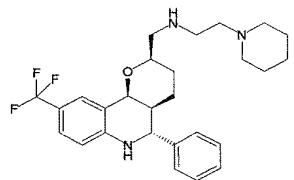
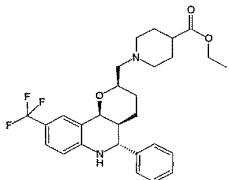
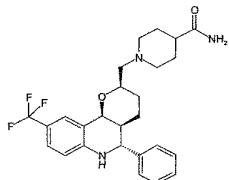
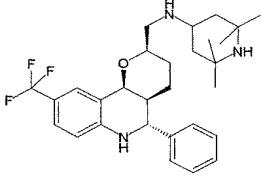
Chemistry 213

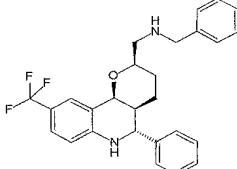
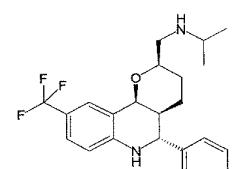
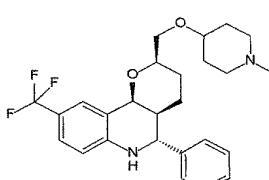
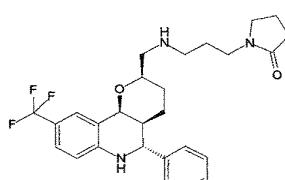
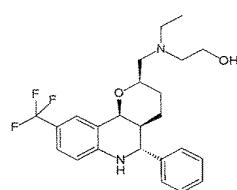
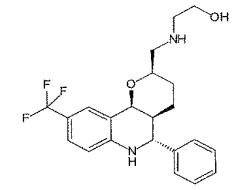
352		(2-Dimethylamino-ethyl)-carbamic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	1,50E-07
Chemistry 212			
353		Pentanoic acid (4aS,5R,10bS)-5-(3-fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	
Chemistry 597			
356		4-Methyl-piperazine-1-carboxylic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	2,70E-07
Chemistry 204			
357		[(2R,4aS,5R,10bS)-5-(4-Fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	9,00E-07
Chemistry 203			
358		[(2S,4aR,5S,10bR)-5-(4-Fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	
Chemistry 202			
359		Pentanoic acid (2R,4aS,5R,10bS)-5-(3-fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	4,40E-07
Chemistry 598			
360		Pentanoic acid (2S,4aR,5S,10bR)-5-(3-fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	
Chemistry 599			

361		Pentanoic acid (2R,4aS,5R,10bS)-5-(2-fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	3,40E-07
	Chemistry 201		
362		Pentanoic acid (2S,4aR,5S,10bR)-5-(2-fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	
	Chemistry 200		
363		[(2R,4aS,5R,10bS)-5-(3-Fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	1,90E-07
	Chemistry 600		
364		[(2S,4aR,5S,10bR)-5-(3-Fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	
	Chemistry 601		
365		[(2R,4aS,5R,10bS)-5-(2-Fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	5,00E-08
	Chemistry 199		
366		[(2S,4aR,5S,10bR)-5-(2-Fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	
	Chemistry 198		
368		Dimethylamino-acetic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	7,00E-08
	Chemistry 196		

562		2-[Ethyl-((2R,4aS,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethanol	1,50E-07
563		2-[Ethyl-((2S,4aR,10bR)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethanol	3,20E-05
564		Methanesulfonic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	1,40E-07
565		(2-Hydroxy-ethyl)-carbamic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	2,50E-08
566		4-Ethyl-piperazine-1-carboxylic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	7,00E-08
567		2-[(2-Hydroxy-ethyl)-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethanol	2,40E-07
568		Diethylamino-acetic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	2,50E-08

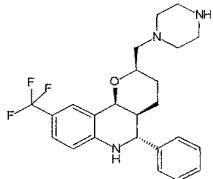
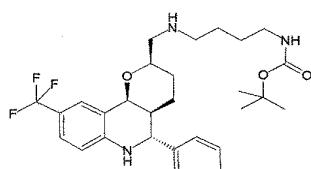
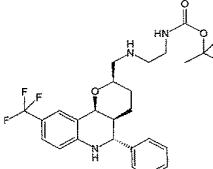
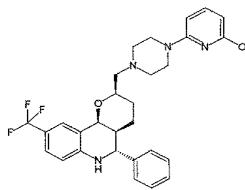
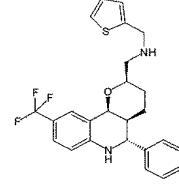
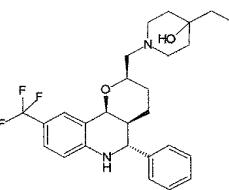
569		{3-[((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-propyl}-carbamic acid tert-butyl ester	7,00E-08
570		[1-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperidin-4-yl]-carbamic acid tert-butyl ester	2,40E-07
571		(2R,4aS,5R,10bS)-2-Chloromethyl-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline	8,10E-07
572		Diethyl-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amine	3,70E-07
573		4-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazine-1-carbaldehyde	3,95E-07
574		(2R,4aS,5R,10bS)-2-(4-Methylpiperazin-1-ylmethyl)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline	2,99E-07
575		Dimethyl-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amine	1,67E-07

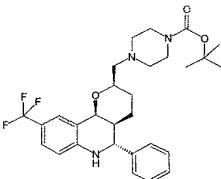
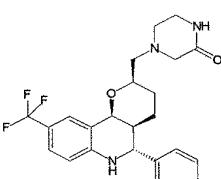
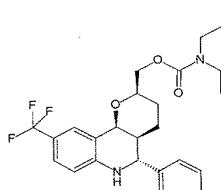
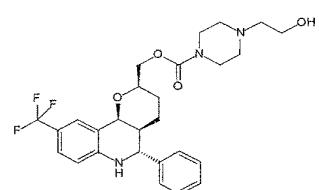
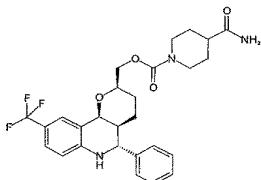
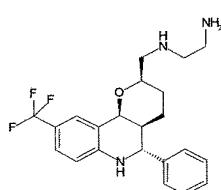
576		C-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl)-methylamine	4,01E-08
577		Methyl-(1-methyl-piperidin-4-yl)-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amine	2,93E-07
578		(2R,4aS,5R,10bS)-2-Morpholin-4-ylmethyl-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline	6,04E-07
579		((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-(2-piperidin-1-yl-ethyl)-amine	1,70E-07
580		1-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperidine-4-carboxylic acid ethyl ester	2,20E-07
581		1-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperidine-4-carboxylic acid amide	2,50E-07
582		((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-(2,2,6,6-tetramethyl-piperidin-4-yl)-amine	2,12E-07

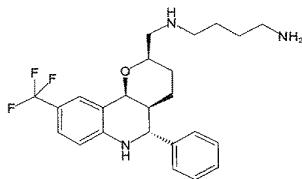
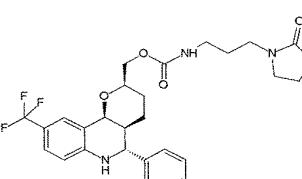
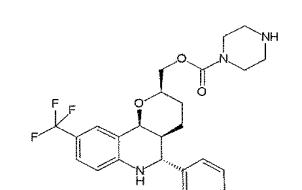
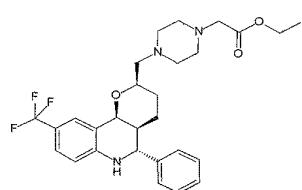
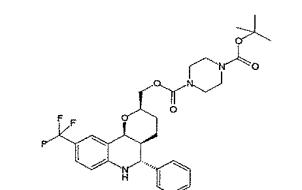
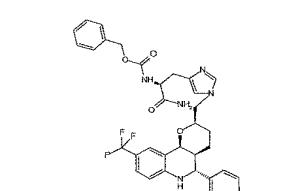
583		Benzyl-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amine	3,30E-07
584		Isopropyl-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amine	1,87E-07
585		(2R,4aS,5R,10bS)-2-(1-Methylpiperidin-4-yl oxymethyl)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline	4,10E-07
586		1-{3-[(2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl]-amino]-propyl}-pyrrolidin-2-one	3,90E-08
587		2-[Ethyl-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethanol	4,90E-07
588		2-[((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethanol	8,48E-08

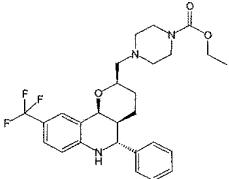
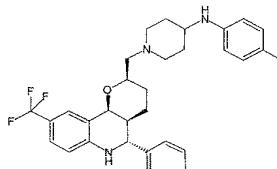
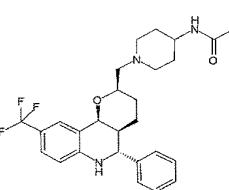
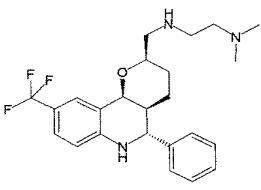
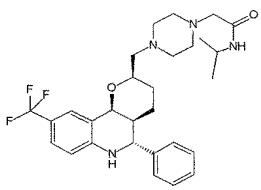
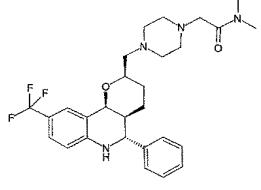
589		2-{2-[((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethoxy}-ethanol	1,45E-07
590		Cyclopentyl-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amine	1,50E-07
591		2-(4-{3-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino}-propyl)-piperazin-1-yl)-ethanol	2,20E-07
592		2-[4-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazin-1-yl]-ethanol	2,10E-07
593		Diethyl-[2-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethoxy)-ethyl]-amine	1,00E-06
594		Dimethyl-[1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-pyrrolidin-3-yl]-amine	2,23E-07
595		1-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperidin-4-ylamine	4,40E-07

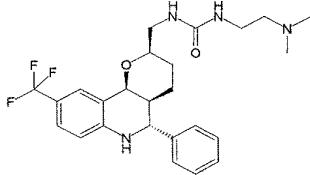
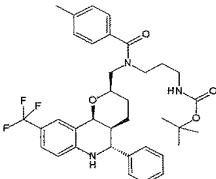
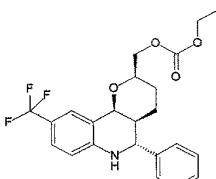
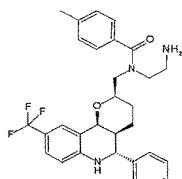
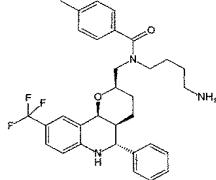
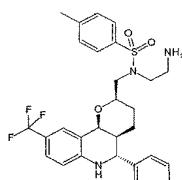
596		[(2R,4aS,5R,10bS)-9-tert-Butyl-5-(4-fluoro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	1,90E-07
597		[(2S,4aR,5S,10bR)-9-tert-Butyl-5-(4-fluoro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	1,00E-05
598		N1-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-propane-1,3-diamine	8,03E-08
599		(2R,4aS,5R,10bS)-2-Imidazol-1-ylmethyl-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline	2,20E-07
600		(2R,4aS,5R,10bS)-5-Phenyl-2-[1,2,4]triazol-1-ylmethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline	2,40E-08
601		N,N,N'-Trimethyl-N'-(2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-ethane-1,2-diamine	2,10E-07

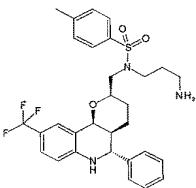
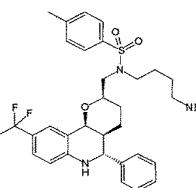
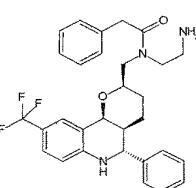
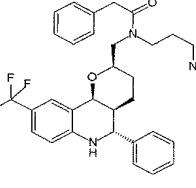
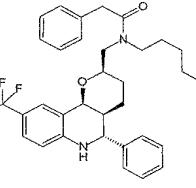
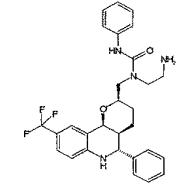
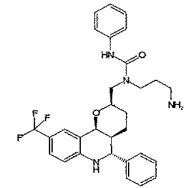
602		(2R,4aS,5R,10bS)-5-Phenyl-2-piperazin-1-ylmethyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline	2,46E-07
603		{4-[((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-butyl}-carbamic acid tert-butyl ester	1,70E-07
604		{2-[((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-ethyl}-carbamic acid tert-butyl ester	1,60E-07
605		6-[4-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazin-1-yl]-pyridin-2-ol	2,00E-07
606		((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-thiophen-2-ylmethyl-amine	1,80E-07
607		4-Ethyl-1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperidin-4-ol	7,90E-08

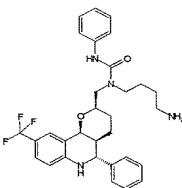
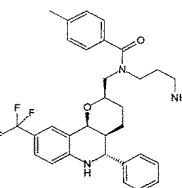
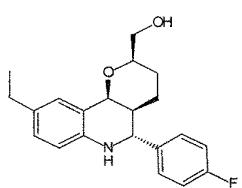
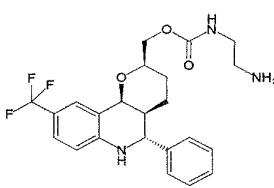
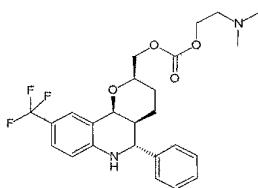
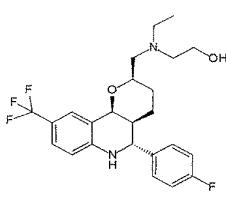
608		4-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazine-1-carboxylic acid tert-butyl ester	1,20E-06
609		4-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazin-2-one	3,20E-07
610		Diethyl-carbamic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	3,40E-06
611		4-(2-Hydroxy-ethyl)-piperazine-1-carboxylic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	2,10E-07
612		4-Carbamoyl-piperidine-1-carboxylic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	3,80E-07
613		N1-((2R,4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-ethane-1,2-diamine	4,93E-08

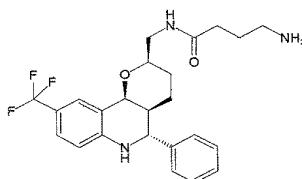
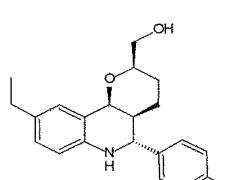
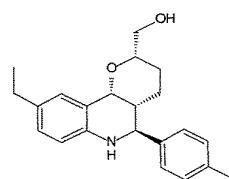
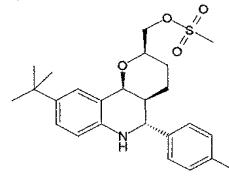
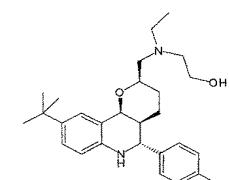
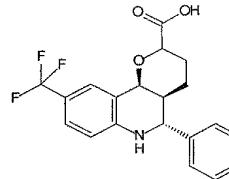
614		N1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-butane-1,4-diamine	2,90E-07
615		[3-(2-Oxo-pyrrolidin-1-yl)-propyl]-carbamic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	4,40E-07
616		Piperazine-1-carboxylic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	4,00E-07
617		[4-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazin-1-yl]-acetic acid ethyl ester	5,30E-07
618		Piperazine-1,4-dicarboxylic acid tert-butyl ester (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	5,30E-06
619		{(S)-1-Carbamoyl-2-[1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-1H-imidazol-4-yl]-ethyl}-carbamic acid benzyl ester	3,50E-07

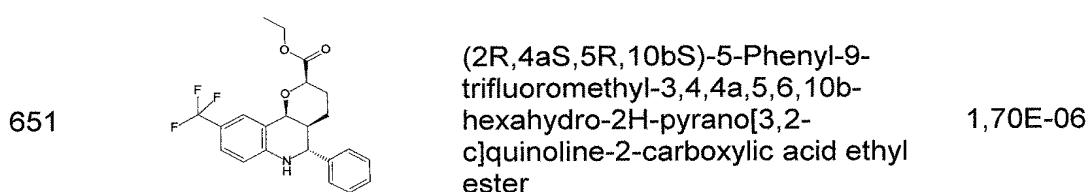
620		4-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazine-1-carboxylic acid ethyl ester	8,80E-07
621		(4-Fluoro-phenyl)-[1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperidin-4-yl]-amine	3,20E-07
622		N-[1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperidin-4-yl]-acetamide	1,50E-07
623		N,N-Dimethyl-N'-(2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-ethane-1,2-diamine	4,64E-08
624		N-Isopropyl-2-[4-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazin-1-yl]-acetamide	3,80E-07
625		N,N-Dimethyl-2-[4-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-piperazin-1-yl]-acetamide	3,30E-07

626		1-(2-Dimethylamino-ethyl)-3-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-urea	3,40E-08
627		{3-[{(4-Methyl-benzoyl)-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-amino]-propyl}-carbamic acid tert-butyl ester	2,10E-06
628		Carbonic acid ethyl ester ((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	3,44E-07
629		N-(2-Amino-ethyl)-4-methyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-benzamide	2,28E-08
630		N-(4-Amino-butyl)-4-methyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-benzamide	1,70E-06
631		N-(2-Amino-ethyl)-4-methyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-benzenesulfonamide	5,00E-08
	537940		

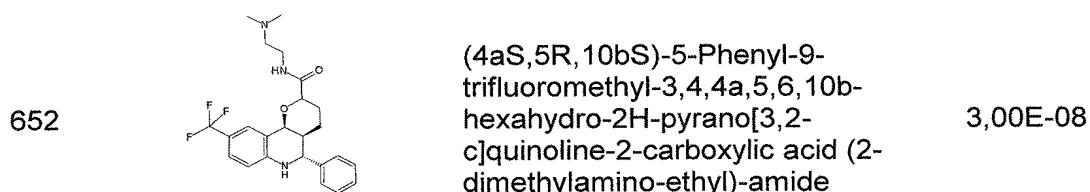
632		N-(3-Amino-propyl)-4-methyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-benzenesulfonamide	7,50E-07
633		N-(4-Amino-butyl)-4-methyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-benzenesulfonamide	1,90E-06
634		N-(2-Amino-ethyl)-2-phenyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-acetamide	1,20E-07
635		N-(3-Amino-propyl)-2-phenyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-acetamide	3,40E-07
636		N-(4-Amino-butyl)-2-phenyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-acetamide	1,70E-06
637		1-(2-Amino-ethyl)-3-phenyl-1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-urea	6,20E-07
638		1-(3-Amino-propyl)-3-phenyl-1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-urea	1,60E-06

639		1-(4-Amino-butyl)-3-phenyl-1-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-urea	3,00E-06
640		N-(3-Amino-propyl)-4-methyl-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-benzamide	8,10E-07
641		[(2R,4aS,5R,10bS)-9-Ethyl-5-(4-fluoro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	4,00E-07
642		(2-Amino-ethyl)-carbamic acid (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	3,90E-07
643		Carbonic acid 2-dimethylaminoethyl ester (2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	9,20E-08
644		2-{Ethyl-[(2R,4aS,5R,10bS)-5-(4-fluoro-phenyl)-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl]-amino}-ethanol	5,30E-07

645		4-Amino-N-((2R,4aS,5R,10bS)-5-phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl)-butyramide	1,70E-07
646		[(2R,4aS,5R,10bS)-9-Ethyl-5-(4-fluoro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	1,80E-07
647		[(2S,4aR,5S,10bR)-9-Ethyl-5-(4-fluoro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-yl]-methanol	9,10E-06
648		Methanesulfonic acid (2R,4aS,5R,10bS)-9-tert-butyl-5-(4-fluoro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl ester	1,10E-06
649		2-{{(2R,4aS,5R,10bS)-9-tert-Butyl-5-(4-fluoro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-2-ylmethyl}-ethyl-amino}-ethanol	1,20E-07
650		(4aS,5R,10bS)-5-Phenyl-9-trifluoromethyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline-2-carboxylic acid	1,10E-05

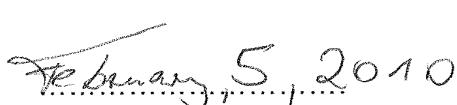


Chemistry 607

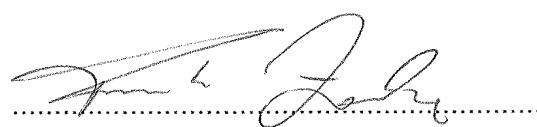


Chemistry 608

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.


February 5, 2010

Date


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Frank Zenke